Synthesis of 2-amino-4H-Chromenes: A Review

Rupnar B.D.*, Rokade P. B., Gaikwad P. D., and Pangrikar P.P.

***Abstract*—**Chromene derivatives are an important class of heterocyclic compounds, widely distributed in natural products. Chromene and its derivatives have also been recognized as one type of 'privileged medicinal scaffolds' due to their unique pharmacological and biological activities. Among various chromene family members, 2-amino-4H-chromenes are especially important for medicinal applications.

***Keywords*—**2-amino-4H-chromene, annulation, Multicomponent reaction, Michael addition.

I. Introduction

2-Amino-4H-Chromenes are an important class of heterocyclic compounds having important biological activities. During the last decade, such compounds had shown interesting pharmacological properties including antimicrobial, [1]antiviral, [2]mutagenicity, [3]antiproliferative, [4]sex pheromone, [5]antitumor [6]cancer therapy [7]and Central nervous system activity.[8]

Multi-component reactions (MCRs) constitute an especially attractive synthetic strategy for rapid and efficient library generation due to the fact that the diversity can be achieved simply by varying the reacting components.

Advantages of multicomponent reactions

- Simple procedures
- High bond forming efficiency
- Time and energy saving
- Low expenditures.

II. Review of Literature

This review will summarize the reported methods for the syntheses of 2-amino-4H-chromene derivatives from the Multicomponent reaction. For the purposes of this review, chromene derivatives will include flavans, flavones and chromones. The synthetic methods in the literature will be compared and contrasted in terms of their generality,selectivity and percentage yields.

S. Makaram and co-workers developed electrochemically induced multi-component condensation of resorcinol, malononitrile, and various aldehydes in propanol in an undivided cell in the presence of NaBr as an electrolyte results in the formation of 2-amino-4H-chromenes in good yields and short reaction time.[9].

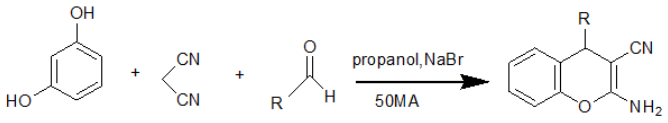

Fig. 1

T. H. Babu et.al.reported an efficient and simple synthesis of highly functionalized azidochromene derivatives. This achieved by Michael addition of a-azido ketones on iminocoumarin derivatives obtained from salicylaldehydes and malononitrile. Synthesized azidochromenes were successfully transformed into triazolylchromenes by the [3+2] cycloaddition reaction.[10].

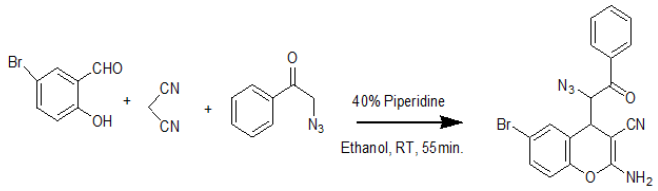

Fig. 2

S.R. Kolla et.al. prepared variety of novel 2-amino-5-hydroxy-4H-chromene derivatives with various substituents on the 4Hchromenering were efficiently synthesized by one-pot reactions of substituted resorcinols and various2-benzylidenemalononitriles in the presence of calcium hydroxide in methanol at room temperature. This simple method provided 2-amino-5-hydroxy-4H-chromenes with high yields under mild reaction conditions.[11].

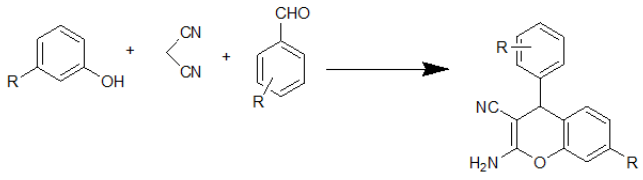

Fig. 3

S. Khaksaret.al.synthesized highly efficient one-pot three-component regioselective synthesis of 2-amino-3-cyano-4H-chromene and tetrahydrobenzo[b]pyran derivatives has been developed with good yield by annulation of aldehydes, malononitrile, and resorcinol or dimedone under reflux

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conditions in 2,2,2-trifluoroethanol without the use of a catalyst or any other additive.[12].

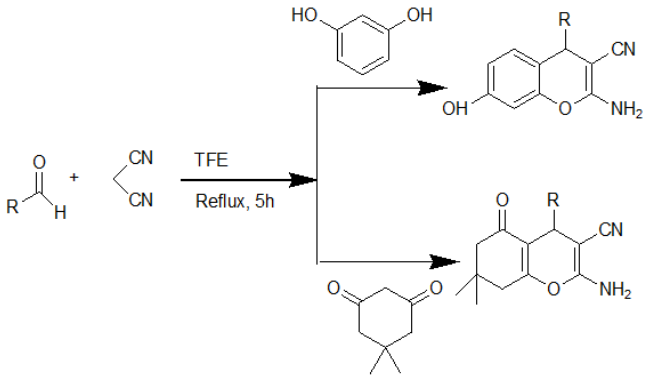
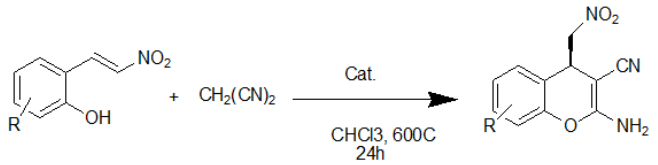


Fig. 4

Recently Yu.Gao.andcoworkers developed organocatalytic enantioselective tandem Michael addition–cyclization of malononitrile to nitroalkenes for the direct synthesis of chiral 2-amino-4H-chromene-3-carbonitrile derivatives was investigated. Good yields and enantioselectivities (up to 91% ee) were achieved. This organocatalytic asymmetric tandem Michael addition–cyclization provides an efficient route toward the synthesis of optically active functionalized chromenes.[13].



Cat- substituted thio urea

Fig. 5

III. Result

These reactions can be run under quite mild conditions and are ideal for the synthesis of chromene derivatives due to their operational simplicity. The development of enantioselective reactions to give nearly optically pure chromene derivatives is a memorable highlight of this review. Future work will undoubtedly focus on transformation of different chromene derivatives

References

[1] Khafagy, M. M.; El-Wahas, A. H. F. A.; Eid, F. A.; El-Agrody, A. M. Fármaco 2002,57, 715–722.
[2] (a) Smith, W. P.; Sollis, L. S.; Howes, D. P.; Cherry, C. P.; Starkey, D. I.; Cobley, N.K. J. Med. Chem. 1998, 41, 787–797; (b) Martinez, A. G.; Marco, L. J. Bioorg.Med.Chem. Lett. 1997, 7, 3165–3170.
[3] Hiramoto, K.; Nasuhara, A.; Michiloshi, K.; Kato, T.; Kikugawa, K. Mutat. Res.1997, 395, 47–56.
[4] Dell, C. P.; Smith, C. W. European Patent Appl. EP 537949; Chem. Abstr. 1993,119, 139102d.
[5] Bianchi, G.; Tava, A. Agric. Biol. Chem. 1987, 51, 2001–2002.
[6] Mohr, S. J.; Chirigos, M. A.; Fuhrman, F. S.; Pryor, J. W. Cancer Res. 1975, 35,3750–3754.
[7] (a) Anderson, D. R.; Hegde, S.; Reinhard, E.; Gomez, L.; Vernier, W. F.; Lee, L.;Liu, S.; Sambandam, A.; Snider, P. A.; Masih, L. Bioorg. Med. Chem. Lett. 2005, 15,1587–1590; (b) Skommer, J.; Wlodkowic, D.; Matto, M.; Eray, M.; Pelkonen, J.Leukemia Res. 2006, 30, 322–331. and references cited therein; (c) Wang, J. L.;Liu, D.; Zhang, Z.; Shan, S.; Han, X.; Srinvasula, S. M.; Croce, C. M.; Alnemeri, E.S.; Huang, Z. Proc. Natl. Acad. Sci. U.S.A. 2000, 97, 7124–7129.
[8] Eiden, F.; Denk, F. Arch. Pharm. WeinheinGer (Arch. Pharm.) 1991, 324, 353–354.
[9] S.Makarem; A. A. Mohammadi , A. R. Fakhari Tetrahedron Letters 49, 2008, 7194-7196.
[10] T. H. Babu, J. Kamalraja, D. Muralidharan, P. T. Perumal, Tetrahedron Letter 52, 2011,4093-4096.
[11] S.R. Kolla, Y.R. Lee; Tetrahedron 67 (2011) 8271-8275.
[12] S.Khoksar ;SamadKhaksar; Ahmad Rouhollahpour, SaeedMohammadzadehTalesh; Journal of Fluorine Chemistry 141 (2012) 11-15.
[13] Yu Gao, Wen Yang, Da-Ming Du;Tetrahedron-assymmetry 23 ,2012,339-344.